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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/538,498

01/09/2006

Xu Zhang

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MORRISON & FOERSTER LLP

12531 HIGH BLUFF DRIVE

SUITE 100

SAN DIEGO, CA 92130-2040

EXAMINER

SNYDER, STUART

ART UNIT

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1648

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/538,498	Applicant(s) ZHANG ET AL.	
	Examiner Stuart W. Snyder	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) 3,4 and 34-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 5-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/29/2005, 12/7/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. Election of Group I, claims 1-41 in the filing of 5/21/2007 is acknowledged.
Further election of the following species in the same filing is acknowledged: Cell, whole blood, paramagnetic substance, 200 nanometers, hydroxyl group, washing, automated process, 10 minutes, eppendorf tube, absence of precipitating procedure, absence of poisonous agent, room temperature, pH 6.0, ion concentration one third [larger than] that of normal whole blood, and low-temperature conserved samples. Claims 1, 2, and 5-33, as amended 6/9/2005, specifically read on the elected group and species and are subject to examination; claims 3-4 and 34-55 are withdrawn from examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 22 recites "eppendorf" tube. A quick review of the Eppendorf web site reveals at least 8 different types of tubes. If volume or the material of the tube is important to the procedure, the limitation of "eppendorf" does not specify these details and renders the claim indefinite.
3. Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. Claim 32 recites "physiological salt water". The phrase has support in the specification (see page 15, line 17) but no definition. Furthermore, there are various physiological salts, e.g., NaCl, KCl, phosphates, citrates, acetates, etc., only some of which have buffering capacity in the specific range of the claim, i.e., 6.5. The limitation of "physiological salt water" does not specify with clarity these details and renders the claim indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-2, 5-9, 11, 13-15, 22, 24-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Antoine, *et al.* The claims are drawn to a method for isolating a cell (leukocyte) from a sample comprising contacting a sample with a magnetic microbead that binds to the target cell not comprising a moiety that binds to the target cell with high specificity and in a chemical environment comprising 3-7 pH, an ion concentration that is about one thirds larger than normal whole blood, and/or a suitable concentration of an anticoagulant especially those named in claim 30, allowing the cell to bind to the magnetic microbead non-specifically or with low specificity, and separating the cell/microbead (conjugate) from the other undesirable sample constituents with magnetic force, washing the conjugate with a saline or PBS buffer having a pH of

about 6.5 and releasing/recovering the cell from the conjugate in a suitable buffer then removing the microbead magnetically, the method taking between 1-20 minutes and conducted in an Eppendorf; further limitations include that the cell is an animal cell, the magnetizable substance is paramagnetic, metallic in composition, a transition metal composition, selected from various named transition metals especially including an iron oxide (Fe_3O_4), the bead is untreated or modified with an organic molecule, the procedure lacks a precipitation step or presence of a poisonous agent, and is conducted at an ambient temperature ranging from about 0° to about 35° C.

Antoine, *et al.* teaches using iron oxide imbedded polyacrylamide-agarose microbeads coated with anti-mouse or anti-rat Ig (an organic molecule) used to isolate mouse or rat lymphoid cells from blood or plasma, magnetically separating the conjugate, washing the cells with PBS buffer (pH 7.4 or about pH 6.5), and eluting the cells from the microbeads then removing the microbeads.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 10, 12, 16, 17, and 22 rejected under 35 U.S.C. 103(a) as being unpatentable over Antoine, *et al* as applied to claims 1-2, 5-11, 13-15, 24-33 above and in further view of Ullman, *et al.* The claims are drawn to the method

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outlined above with the additional limitations: Microbead size between about 5×10^{-9} and 5×10^{-5} m, the microbead is modified to comprise a hydroxyl group, the sample selected from among various clinical specimen types specifically including blood, and the method completed within about 1 min. to about 20 min. Although Antoine, et al teaches one of the non-elected species (cell cultures), it does not teach the aforementioned limitations. Ullman, *et al.* teaches use of a microbead sized between 2×10^{-8} and 1×10^{-4} m (a range that overlaps with the range of claim 10, see column 6, lines 65 ff), polymeric microbeads comprising hydroxyl groups (see column 7, lines 32 (alcohol) and 34 (free hydroxyl)), a clinical specimen (see, column 16, lines 62-64), a sample comprising blood (see column 13, lines 39-41), and the time of completing the method of 15-85 sec (this overlaps with the range of 1-10 min of claim 22; see column 18 lines 18-31 especially line 27).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Antoine, *et al.* by using the limitations described above as taught by Ullman, *et al.* The skilled artisan would have been motivated to do so because both methods have a common goal of isolating cells and it is inherently obvious to combine features of similar methods. There would have been a reasonable expectation of success, given the success of the method, as taught by Ullman, *et al.* (see, especially the Examples section of the Patent). Thus, the invention of claims 10, 12, 16, 17, and 22 was clearly

prima facie obvious to one of ordinary skill in the art at the time the invention was made.

6. Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antoine, et al as applied to claims 1-2, 5-11, 13-15, 24-33 above and in further view of Brinchmann, *et al.* Antoine, et al does not teach further separation of biological material, especially an oligonucleotide that is subsequently amplified using an automated procedure. Brinchmann, et al. teaches a method of separating HIV-infected cells from whole blood, washing the cell, isolating either HIV RNA or HIV DNA and amplifying the oligonucleotides (PCR of *pol* gene). Brinchmann, et al. does not specifically teach an automated procedure, however it is inherently obvious to automated a manual method (see MPEP 2144.04, quoted below).

In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) (Appellant argued that claims to a permanent mold casting apparatus for molding trunk pistons were allowable over the prior art because the claimed invention combined "old permanent-mold structures together with a timer and solenoid which automatically actuates the known pressure valve system to release the inner core after a predetermined time has elapsed." The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Antoine, et al. by using the limitation of the claims as taught by Brinchmann, et al. The skilled artisan would have been motivated to do so to detect specific nucleic acid sequences of the isolated cells as taught by Brinchmann, et al. There would have been a reasonable

expectation of success, given the success of Brinchmann's group. Thus, the invention of claims 18-21 was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

7. No claims are allowed.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart W. Snyder whose telephone number is (571) 272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stuart W Snyder
Examiner
Art Unit 1648

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